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# Tulane University Medical Center

## 1995-1996 Research Progress

Petrochemical Wastes: Risks and Remediation

P42 ES05946

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**Project 1: Assays of Genotoxicity (Ehrlich, Mullin)**

This project is developing sensitive methods for quantitating genotoxin-induced gene rearrangements. It has been shown that a DNA demethylating agent can stimulate the formation of breast-cancer associated chromosomal rearrangements in cultured human cells. This suggests that DNA demethylation, which frequently occurs during cancer formation, may be an important source of karyotypic instability in cancer. Karyotypic instability often results in activation of oncogenes or gene dose imbalances that contribute to tumor formation and tumor progression.

**Project 4: Chelating Agents for Extracting Toxic Metals (Pintauro)**

This project is directed towards the use of chelating agents to enhance the *in-situ* extraction of heavy metals such as cadmium, lead, zinc, and copper from soils at Superfund waste sites by surfactant flushing and electrokinetic techniques. One component of this project involves the development and testing of a mathematical computer model for the time-dependent fluid flow and ion mass transfer processes that occur during electrokinetic reclamation of Cd-contaminated soil. In the model, differential equations which describe mass transport and fluid flow in a porous clay bed have been combined with expressions for a pH-dependent clay surface charge and chemical reactions between soluble Cd ions/Cd complexes and the clay surface. A finite element numerical solution scheme has been used to solve the coupled rectilinear partial and ordinary differential equations. In its present form, the model simulates water flow, proton, hydroxyl ion, and soluble lead species movement (electromigration, diffusion, and convective mass transfer) in a clay bed under constant applied current operating conditions.

The second component of this research project focused on the use of emulsions for the purpose of removing toxic substances from soil. Successful experiments of flowing oil-in-water emulsions through sand-packed beds revealed several phenomena dictating the mechanism of emulsion transport through soil. The role of key surfactants was investigated for chelating heavy metals, and for facilitating/obstructing emulsion flow through porous media. Also under this grant, a study was undertaken to explain the dynamics of solubilization of emulsion oils in surfactant-stabilized emulsions.

**Project 5: Cell Biology of Mutagenic and Cytotoxic Lung Injury (Brody)**

In a rodent model of pulmonary fibrosis, a single inhalation exposure to asbestos fibers initiates the

events that generate a fibrotic scar at the sites of fiber deposition in the lung. The goal of this research is to establish which of the early cellular and molecular events post-exposure to asbestos correlate with the subsequent fibrotic response. Three cohorts of rats were unexposed/exposed to aerosolized chrysotile asbestos, or exposed to aerosolized iron spheres. At various times post-exposure, animals were sacrificed and the lungs were evaluated by immunostaining with a monoclonal antibody specific for p53. The unexposed and iron-exposed animals exhibited no p53 immunostaining at any point in time. Exposure of the animals to asbestos activated expression of p53 at the predicted sites of fiber deposition, the bronchiolar-alveolar duct bifurcations. p53 immunostaining appeared by 24 hours post-exposure, reached a maximum at the 8-day time point, and waned by 14 days post-exposure. The significance of p53 during scarring of the lung has yet to be established. p53 functions as a transcription factor that regulates DNA replication, DNA repair, and apoptosis. Clearly, the ability of p53 to mediate these functions in a developing fibrotic lesion would have profound effects upon the regenerative capacity of the lung. Double immunofluorescent staining for p53 and PCNA indicates that both proteins are expressed in the same cell population. This observation is consistent with data indicating that p53 activates expression of the PCNA promoter, and suggests that inhalation exposure to asbestos may induce a genotoxic response in pulmonary cells.

**Project 6: Alterations in Immunoneuroregulation by Environmental Agents (Salvaggio)**

The objectives of this project are to assess more fully the effect of selected chemicals on the immune and central nervous systems. These studies have involved a dual experimental approach assessing the effects of these materials *in vitro* on cultured cells, and *in vivo* in a rodent model. Emphasis will be placed on the effect of these agents on cytokine production, cell surface receptor activity, and cytokine-induced CNS neurohormone production. Over the past year, the effects of two different methylmercury compounds on the immune system of the newborn rat after indirect exposure were investigated. This research found a significant decrease in the Natural Killer (NK) cytotoxic activity in rats exposed via placenta and lactation to methylmercury chloride.

**Project 7: Passive Sampling of Airborne Contaminants (Rando)**

A multicompartment sampler was designed and evaluated in the laboratory for boundary layer-resistant passive sampling. The sampler consists of three cylindrical chambers each of diameter 40.9 mm and cross sectional area (A) of 13.14 cm2, and of depths (L) of 12.0, 20.8, and 31.3 mm. The three chambers share a common sampling face, and use charcoal as an absorbent material. The device was tested against xylene vapor under low wind speed conditions (3 feet/minute and 12 feet/minute) and three orientations (wind impinging at 90 to the sampler face, wind parallel to the face, and wind perpendicular to the face but coming from behind). After determining the mass transfer rate (m/t) of each compartment independently by gas chromatographic analysis, a plot of t/m versus L/DA for the three compartments yielded a line whose intercept was equal to the ratio of the boundary layer depth to DA, and the slope was the exposure concentration. The predicted concentration from this algorithm exhibited a bias ranging from 71 to 464% in comparison to the true exposure concentration. The most significant error was associated with the wind directed at the back of the sampler. Wind flowing parallel across the sampling face resulted in errors of only 3%. The data also suggested that the observed error was very sensitive to the precision of analysis of the mass transfer rates of the individual compartments.

**Project 8: Chronic Airways Effects of Chemical Exposures in Asthmatics (Glindmeyer)**

This project is investigating the role of host susceptibility on respiratory response to occupational airborne irritant chemical exposures from plants where chlorine and chlorine dioxide are the primary irritants. A large population (n = 15,000+) of individuals not exposed to workplace inhalants has been identified from the overall cohort under Tulane centralized respiratory health surveillance. These

individuals have been followed with the same standardized respiratory health data collection procedures, and are located at 62 sites scattered throughout the United States. At this time, the matching of the specific sites to EPA ambient air sampling data is being attempted. This additional cohort will allow evaluation of respiratory health effects following environmental exposures (NOx, SOx, Ozone, CO, particulates) on the general population, including susceptible individuals, after adjusting for smoking.

**Project 9: Oxidation of Organic Chemicals by Genetically-engineered Micro-organisms (Alworth)**

This project is utilizing genetic engineering to generate *Escherichia coli* cells that will express mutated cytochrome P450BM-3 enzymes capable of catalyzing the oxidation of a variety of hazardous organic chemicals found at hazardous waste sites. The substitution of a single amino acid residue (phe87) with an alternative residue (gly) changes the substrate and reaction specificity of the bacterial P450 102 protein. Protein activity is transformed from a catalyst that causes the -1, -2 or -3 hydroxylation of fatty acids into a catalyst that facilitates the molecular oxygen-dependent hydroxylation of polycyclic aromatic hydrocarbons (PAH), such as pyrene and benzo[a]pyrene. Since such PAH are environmental pollutants, this establishes the possibility of using a mutated bacterial P450 protein to catalyze the oxidative metabolism of polluting PAH found in the environment.

**Exposure Assessment Core (Rando)**

A nine-month inhalation exposure of transgenic mice at a target level of 100 ppm benzene was completed. Core personnel were responsible for daily operation of the chamber, verification of exposure level by continuous monitoring and grab sample analysis in the laboratory, weekly weighings of the test and control animals, and daily inspection of the animals for signs of illness, etc. The mean exposure level was 102 ppm, with a coefficient of variation of 30%.

Exposure surveys for chlorine and chlorine dioxide were conducted at two paper/pulp mills. Twenty-seven workers were monitored over an entire work shift using the Tulane passive sampler. After collection, the samples were shipped back to Tulane and analyzed by ion chromatography.

Preliminary investigation of a solid sorbent for collection and measurement of reduced sulfur gases was completed. Y52 and X13 zeolite molecular sieves, untreated as well as doped with various transition metal ions, were evaluated for collection of dimethyl sulfide and dimethyldisulfide vapors. The metal-doped zeolites showed good retention of the vapors, but were not completely reversible due to apparent reaction with the collected sulfur gases. A mixture of the two untreated molecular sieves exhibited the best overall performance in terms of capacity and recovery under thermal desorption.

**Training Core (White)**

Due to the approaching end of this Superfund grant, no new students were accepted into the Training Core's combined BS/MSPH degree program for the spring semester. Those graduate students already enrolled in the program have continued their studies, and will be graduating in May, 1996.